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# Minor physical anomalies are more common in schizophrenia patients with the history of homicide



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## ABSTRACT

Minor physical anomalies may be external markers of abnormal brain development, so the more common appearance of these signs in homicidal schizophrenia might suggest the possibility of a more seriously aberrant neurodevelopment in this subgroup. The aim of the present study was to investigate the rate and topological profile of minor physical anomalies in patients with schizophrenia with the history of committed or attempted homicide comparing them to patients with schizophrenia without homicide in their history and to normal control subjects. Using a list of 57 minor physical anomalies, 44 patients with the diagnosis of schizophrenia were examined with the history of committed or attempted homicide, as a comparison 22 patients with the diagnosis of schizophrenia without the history of any kind of homicide and violence and 21 normal control subjects were examined. Minor physical anomalies are more common in homicidal schizophrenia patients compared to non-homicidal schizophrenia patients and normal controls, which could support a stronger neurodevelopmental component of etiology in this subgroup of schizophrenia. The higher rate of minor physical anomalies found predominantly in the head and mouth regions in homicidal schizophrenia patients might suggest the possibility of a more seriously aberrant brain development in the case of homicidal schizophrenia.

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## 1. Introduction

A number of studies have reported a positive association between schizophrenia and violence (Fazel et al., 2009), while in a recent review and meta-analysis Witt et al. (2013) identified dynamic (modifiable) risk factors as hostile behavior, recent drug and alcohol misuse and non-adherence to medication and a number of static factors, the strongest of which were criminal history factors, behind aggression and violence in schizophrenia. Aggression and violence in schizophrenia can be explained by psychopathological and clinical characteristics, but distinct neurobiological mechanisms also may play a role, however only a few studies have addressed the neurobiology of aggression in schizophrenia (Soyka, 2011). As many data indicate that aberrant neurodevelopment underlines schizophrenia, data from neuroimaging studies on schizophrenia patients with and without aggression are interesting, as frontal and temporal lobe abnormalities are found consistently in aggressive patients with the

diagnosis of schizophrenia (Soyka, 2011). Puri et al. (2008) reported results of an MRI study that compared structural changes in schizophrenia patients with and without aggression. Schizophrenia patients with violence were found to have reduced gray matter volumes. Soyka (2011) reviewed magnetic resonance imaging studies and reported on structural abnormalities in violent and aggressive schizophrenia patients, as reduced whole brain and hippocampus volumes (Barkataki et al., 2006), disturbed connectivity between the orbito-frontal cortex and the amygdala (Hoptman et al., 2002) and structural abnormalities in the amygdala (Wong et al., 1997). Most studies have been performed in clinical samples with aggression as measured by psychopathological scales, fewer studies in schizophrenia patients with homicide (Soyka, 2011)

Minor physical anomalies (MPAs) are mild and insignificant errors of morphogenesis which have a prenatal origin and may bear major informational value for diagnostic, prognostic and epidemiological purposes. The presence of minor physical anomalies is a sensitive physical indicator of embryonic development. Since both the central nervous system and the skin derived from the same ectodermal tissue in utero, minor physical anomalies may be external markers of abnormal brain development. Minor physical anomalies are considered

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to develop during the first and/or early second trimester of gestation (Méhés, 1988; Pinsky, 1985; Tényi et al., 2004, 2009) and represent potentially valuable indices of disturbances in early neurodevelopment. Once formed they persist into adult life and are readily detected on visual examination of the particular body area. Minor physical anomalies have been found with increased frequency in various neuropsychiatric illnesses (Waldrop and Goering, 1971; Méhés, 1988; Csábi et al., 2008), schizophrenia (Gualtieri et al., 1982; Lohr and Flynn, 1993; Lane et al., 1997; Trixler et al., 1997, 2001; Akabaliev and Sivkov, 2007; Sivkov and Akabaliev, 2003; Weinberg et al., 2007) and affective disorders (Tényi et al., 2009).

As we (Trixler et al., 1997; Trixler and Tényi, 2000; Trixler et al., 2001; Tényi et al., 2009) and others (Akabaliev and Sivkov, 2007) have discussed earlier, a clear distinction between morphogenetic events developing during and after organogenesis is needed. Minor malformations are always abnormal and are qualitative defects of embryogenesis, which arise during organogenesis. All malformations are developmental field defects and usually they are all-or-none anomalies. In contrast phenogenetic variants are quantitative defects of final morphogenesis and arise after organogenesis. Morphologically phenogenetic variants are the exact equivalents of normal anthropometric variants. Using a list of minor physical anomalies containing 57 minor signs collected by Méhés (1988), previously we have studied the prevalence of minor physical anomalies in patients with schizophrenia, alcohol dependence and major depression (Trixler et al., 1997, 2001; Tényi et al., 2004), and recently the list and detailed definitions has become also acceptable for researchers, who wish to adapt our suggested modifications for the investigation of minor physical anomalies (Trixler et al., 2001).

Minor physical anomalies may be external markers of abnormal brain development, so the more common appearance of these signs in homicidal schizophrenia might suggest the possibility of a more seriously aberrant neurodevelopment in this subgroup of the disorder. As no study has been published yet on the prevalence of MPAs in schizophrenia patients with the history of homicide, the aim of the present study was to investigate the rate and topological profile of minor physical anomalies in patients with schizophrenia with the history of committed or attempted homicide comparing them to patients with schizophrenia without homicide in their history and to normal control subjects. The following hypotheses have been tested: (1) minor physical are more common in homicidal schizophrenia patients compared to non-homicidal schizophrenia patients and normal controls, which could support a stronger neurodevelopmental component of etiology in this subgroup of schizophrenia and (2) a higher rate of minor physical anomalies is found predominantly in the head and facial regions in schizophrenia patients with the history of committed or attempted homicide compared to non-homicidal schizophrenia patients and normal controls, pointing at a possible role of aberrant brain development in the case of homicidal schizophrenia.

## 2. Material and methods

### 2.1. Study subjects

Using a list of 57 minor physical anomalies collected by Méhés (1988), 44 patients with the diagnosis of schizophrenia were examined with the history of committed or attempted homicide. All of these patients were treated in the Forensic Psychiatric Mental Institution (Budapest, Hungary) during the evaluation of the study. As a comparison 22 patients with the diagnosis of schizophrenia were examined, without the history of any kind of homicide and violence, while 21 normal control subjects were also observed for minor physical anomalies. The diagnoses of the patients were evaluated independently by two experienced psychiatrists according to the DSM-IV-TR (*Diagnostic and Statistical Manual of Mental Disorders*, 2000). All available clinical information and data were obtained from structured clinical interviews. In the compared schizophrenia group and the normal control group persons with antisocial behavior, impulse control disorder, personality disorder or any other neuropsychiatric disease were excluded.

### 2.2. Examination of minor physical anomalies

We have used the Méhés Scale for evaluation of minor physical anomalies, which includes 57 minor signs (Trixler et al., 2001, 2009). Minor physical anomalies are connected to body regions for comparison and analysis of data. A clear differentiation between minor malformations and phenogenetic variants were introduced, the scale and detailed definitions were published earlier (Trixler et al., 2001). All participants gave informed consent, the study was performed in accordance with the Declaration of Helsinki and was evaluated following institutional guidelines. Two examiners (Györgyi Csábi, Tamás Tényi) investigated all the patients and controls separately. The raters were trained by Professor Károly Méhés, and they participated earlier in many minor anomaly studies, they have a long clinical experience in dysmorphology. The examination of minor physical anomalies was done qualitatively (present or absent) without scores being used, but where it was possible, measurements were taken with callipers and tape to improve the objectivity of examination.

### 2.3. Statistical analysis

Before the statistical analyses interrater reliability was tested and the kappa coefficient was  $> 0.75$  for all items. Statistical analyses were carried out by applying the Kruskal–Wallis-test for the simultaneous comparison of the three groups, Mann–Whitney *U*-test for the comparison of two groups with each other. Comparing the three groups by body regions *z*-test was introduced, because of multiple comparisons with Bonferroni correction. 2-sided Fisher's exact tests were used to compare two groups with each other by body regions, the level of significance chosen was  $p < 0.025$ . Odds ratios were calculated with 95% confidence intervals. For the analysis of the frequency of each individual minor physical anomalies the two-sided Fisher's exact probability test was used, the level of significance chosen was  $p < 0.025$ . All the statistical analyses were done by the use of SPSS Version 21.

## 3. Results

We should consider as a robust finding that between the three groups a statistically highly significant difference rate could be detected in the prevalence of minor physical anomalies using the Kruskal–Wallis test ( $p < 0.001$ ). Also the comparison of two groups with the Mann–Whitney–*U*-test showed significant differences between them (homicidal schizophrenia patients: mean rank: 39.80 versus non-homicidal schizophrenia patients: mean rank: 20.91,  $p < 0.001$ , homicidal schizophrenia patients: mean rank: 43.35 versus normal controls: mean rank: 11.31,  $p < 0.001$ , non-homicidal schizophrenia patients: mean rank: 31.75 versus normal controls: mean rank: 11.79,  $p < 0.001$ ). The *z*-test comparison of the three groups by body regions confirmed that concerning the ear region, the two schizophrenia groups differed from the control group but not from each other, on the results of the head region the homicidal schizophrenia group was different from both the non-homicidal schizophrenia group and the normal control group, concerning the mouth the homicidal group was different from the non-homicidal schizophrenia group, analyzing the trunk data the non-homicidal group differed from the normal control group, while concerning the legs the homicidal group was different from the normal group. The significant difference between group data of the 2-sided Fisher's exact test comparisons and the Odds ratio results are shown in Table 1. Homicidal schizophrenia patients showed a higher frequency of MPAs in the head and the mouth regions compared to non-homicidal patients, higher rates of MPAs could be seen in the ear, head, eye and leg regions among homicidal schizophrenia patients compared to normal control subjects, while non-homicidal schizophrenia patients showed a higher frequency of MPAs in the ear region compared to normal controls. The results of comparisons of individual MPAs among the three groups are shown in Table 2. Two minor malformations (flat occiput, double posterior hair whorl) were more prevalent in the homicidal schizophrenia group compared to the schizophrenia patients without aggression and violence, four minor malformations (flat occiput, double posterior hair whorl, furrowed tongue, and Sydney line) appeared more

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